



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,075	12/20/2001	Gary S. Gray	RPN-001CN	1776
959	7590	05/07/2004	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			HELMS, LARRY RONALD	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 05/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/027,075	GRAY ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 56-59, 61-63, 65, 67, 69 and 92-94 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 56-59, 61-63, 65, 67, 69 and 92-94 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. Claim 56 has been amended and claim 66 has been canceled.
2. Claims 56-59, 61-63, 65, 67, 69, 92-94 are pending and under examination.
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
4. The following Office Action contains some NEW GROUNDS of rejection.

### ***Oath/Declaration***

5. The oath or declaration is still defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:  
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specifically the citizenship of Kashi Javaherian has been written in.

It is acknowledged that a new oath will be forthcoming but until it is submitted the objection is maintained.

### ***Rejections Withdrawn***

6. The rejection of claims 56-59, 62, 65-67 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendments to the claims.

***Response to Arguments/NEW GROUND of rejection***

6. The rejection of claims 56-59, 61-63, 65, 67, 92-94 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,444,792 is maintained.

The response filed 3/3/04 did not address this rejection and as such the rejection is maintained.

7. The rejection of claims 56-59, 65, 67, 69, 92, and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linsley et al (U.S. Patent 5,434,131, filed 5/26/93, IDS 1 ½ ) and further in view of Gillies et al (Hum. Antibod. Hybridomas 1:47-54, 1990, IDS 1 ½ ) and Freeman et al (U.S. Patent 6,130,316, filed 7/26/94, IDS 1 ½ ) and Canfield et al (J. Exp. Med. 173:1483-1491, 1991, IDS 1 ½ ) and Lund et al (J. Of Immunol. 147:2657-2662, 1992, IDS 1 ½ ) and Duncan et al (Nature 332:738-740, 1988, IDS 1 ½ ) is maintained.

The response filed 3/3/04 has been carefully considered but is deemed not to be persuasive. The response states that the CTLA-Ig fusion protein of the prior art lacks any established need for modification of the then existing CTLA-Ig fusion (see page 9 of response). In response to this argument, Freeman et al clearly teaches modifications to the CH2 domain which are involved in Fc binding (see column 56-57). The response further states that Gillies teach deletion in the CH2 had an effect on the antigen binding properties of the molecule and one skill in the art would conclude that modifications to

Art Unit: 1642

the Fc region might adversely affect the activity of the CTLA4 molecule (see page 9-10 of response). In response to this argument, the molecule of Gillies actually had an increase in binding function which would motivate someone skill in the art to modify the CH2 region. The response states that claims 61-63 and 69 are not obvious because the claims require a CH1 domain. In response to this argument, it is true and that is why these claims are not included in the rejection.

The response states that Linsley molecules are effective without modification and Linsley is devoid of any teaching or suggestion to modify the CTLA-Ig fusion protein (see page 10 of response). In response to this argument, the motivation to alter the molecules is from the secondary references.

The response states Freeman does not disclose why the modifications are desirable or modifications reduce or eliminate Fc mediated receptor activity (see page 11). In response to this argument, Freeman specifically teaches replacement of CH2 amino acids for their ability to bind to Fc. This replacement would result in reducing the Fc mediated response and in view of Canfield who teaches amino acids in the CH2 domain effect the Fc receptor binding, it would have been obvious to substitute the amino acids.

The response states that Gillies, Canfield, and Lund teaches whole antibodies and Gillies disclosure is not of direct benefit in applications of the present invention. In response to this argument, the benefit of Gillies can and would be benefit in the molecules of Freeman because Freeman as well as Canfield teach amino acid substitutions and these molecules can be used in applications where loss of effector

Art Unit: 1642

functions is desirable as indicated in Gillies. The art of Canfield, Lund, and Duncan are cited for teaching modifications in the CH2 domain and hinge at the time of the claimed invention. It was known that these modifications would effect Fc binding and as such elimination of such functions was desirable as indicated in Freeman who teaches CTLA-Ig fusions and not whole antibodies. It is obvious to use the modifications in the prior art and apply them to the molecules of Lindley and Freeman.

### ***Conclusion***

8. No claims are allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.
10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette,

Application/Control Number: 10/027,075

Page 6


Art Unit: 1642

1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832



LARRY R. HELMS, PH.D.  
PRIMARY EXAMINER